EXPERIENCE WITH THE METHOD OF GRABECKI AND COWORKERS FOR THE DETERMINATION OF URINE DELTA-AMINOLEVULINIC ACID IN THE PREVENTION OF LEAD POISONING

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16. Abstract

Our experiences with the method for the rapid determination of δ-ALA in urine given by Grabecki and coworkers are described. This method is less expensive than the method of Mauzerall and Granick and therefore available in screening of lead-exposed workers.

According to this method proposals are made in order to establish the normal values and the acceptable limit values of δ-ALA-excretion in urine.

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I.

EXPERIENCE WITH THE METHOD OF GRABECKI AND COWORKERS FOR THE DETERMINATION OF URINE DELTA-AMINOLEVULINIC ACID IN THE PREVENTION OF LEAD POISONING

W. Müller and G. Holzapfel

Prophylaxis of lead poisoning continues to be of the greatest interest in industrial medicine. As there are no manifest clinical changes in the preventive area, various methods of laboratory investigation are employed to judge the effect of lead. But it is still debatable, which methods are practically usable here. While in the opinion of Americans the degree of danger from lead can be judged exactly only by means of lead analyses in air, blood and urine, in Europe we are more of the opinion that the extent of biological reactions should be the primary measure for prophylactic medical treatment. This viewpoint is also expressed in the findings of the "Conference on Inorganic Lead" which was held in Amsterdam in November, 1968 [6]. Although there are different opinions about the specificity of the various biological /288 parameters, there is scarcely any more doubt about the practicality of determining delta-aminolevulinic acid in the urine. Increased ALA excretion in the urine is one of the earliest symptoms of the disturbance in heme synthesis caused by lead. It also reflects quite accurately the current influence of lead.

The original method of ALA determination of Mauzerall and Granick [5] proved to be too expensive for routine investigations.

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* Numbers in the margin indicate pagination in the original foreign text.

Therefore, rapid methods have recently been developed to make the determination of ALA usable on a larger scale for monitoring investigations. We wish to report here on our experience with the rapid determination method of Grabecki et al.[3].

We add some brief explanations, to the extent that they are needed for understanding. (Details should be referred to in the original of Grabecki).

This rapid method is a simplified modification of the original method of Mauzerall and Granick, in which the time-consuming isolation of ALA by ion exchange is left out. In our experience, one needs 6 hours for determination of ALA by the original method and the preparations which it requires. The number of urine samples is less significant, because more of them can be processed simultaneously. ALA determination with the rapid method requires only about 1 hour. To be sure, we must assume that the values found with the rapid method are higher than with the original method because interfering substances such as amino acids, ammonia and glucosamine [1,8] are included in the result. Grabecki et al. found, first in a model experiment and later with subjects exposed to lead, that there was a linear relation between the results of the two methods. This relation was expressed by the function: $y = 0.25 + 0.96x$ (x = ALA by the original method, y = ALA by the rapid method, both in mg/100 ml; range up to 5.5 mg ALA/100 ml according to the original method).

With 81 test subjects (19 unexposed and 62 exposed painters and rust removers) we have performed parallel determinations of ALA by both methods and have compared the results. For the study we used urine specimens which were always voided at 8 AM. This method proves entirely sufficient in our experience. The use of morning urine or 24-hour urine can only be practical for

stationary installations.

We have established the regression equations for the relation of the original method to the rapid method and for the relation of the rapid method to the original method. The first equation is $y = 262 + 0.97\ x$ (x = ALA by the original method, y = ALA by the rapid method, in µg/100 ml urine, range up to 2,000 µg ALA per 100 ml, variation 458; Figure 1.) It is almost identical /289

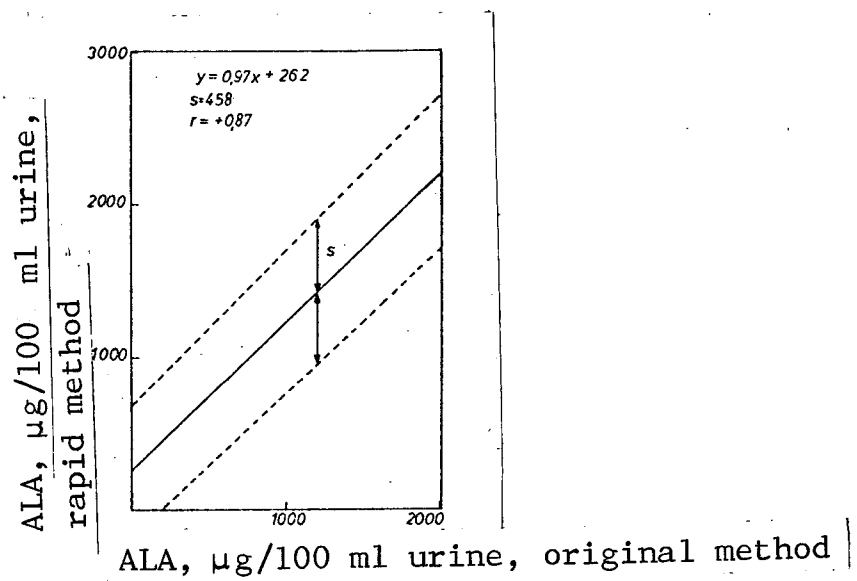

Figure 1. The relation between the results from parallel determinations of delta-aminolevulinic acid excretion by the method of Mauzerall and Granick (x) and according to Grabecki et al. (y) in the urine of 89 subjects.

with the regression equation of Grabecke et al; the differences are due solely to the differing dimensions for the amount (µg instead of mg).

To be sure, we found this relation valid only for a range up to 2,000 µg ALA/100 ml urine (Grabecki et al., up to 5,500 µg/100 ml). Above the vicinity of 2,000, we found

that our values with the rapid method approximated those from the original method. We do not consider this as a necessary disadvantage because, as we shall see below, values above 2,000 µg/100 ml can no longer be considered as lying within the tolerance range. Often other lead signs are already present in such cases (beginning anemia), which make a change in work place necessary. But even if such high ALA values occur without other symptoms, they nevertheless require short-term checks.

We must also consider the following: Grabecki et al. have demonstrated the great precision of their rapid method; but in practice, one must figure on a large range of variation in comparing the results of the two methods, particularly at high values.

The Polish authors [3] have not stated the dispersion about their regression line, but it can be estimated quite well from the plotted measurements. It could be about 1,500 in the range from 2,000 - 5,000 µg/100 ml urine.

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Our second regression line (relation of the rapid method to the original method) is $y = 0.77\,x - 77$ (x = ALA by the rapid method, y = ALA by the original method, in µg/100 ml, range up to 2,700 µg ALA/100 ml urine by the rapid method; dispersion 409; Figure 2.)

We wish to state briefly our opinion on the normal value which applies to the rapid method and the still acceptable upper limit of ALA excretion in the urine:

The pertinent literature states normal values both for ALA excretion in a certain time period (usually 24 hours) and for a certain amount of urine (usually 100 ml). The normal value given for 24 hours varies between 2,100 and 4,000 µg [2]. The

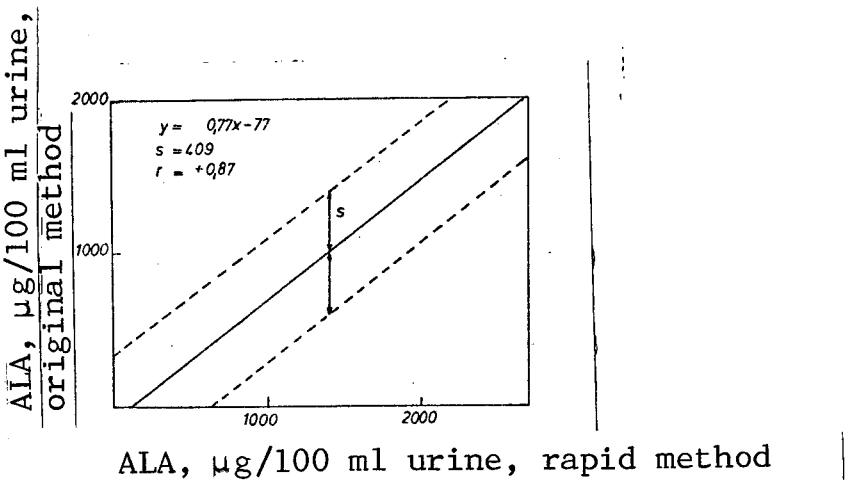

Figure 2. The relation between results from parallel determinations of delta-aminolevulinic acid excretion by the method of Grabecki et al.(x) and of Mauzerall and Granick (y) in the urine of 89 subjects.

normal value for 100 ml of urine stated by Haeger-Aronson [4] is 290 ± 140 µg. Both statements refer to findings with the original method. On the basis of the latter value, the normal value for the rapid determination method, in our experience, would be about 700 ± 450 µg/100 ml. The upper normal limit is, accordingly, 1,150 µg/100 ml. With this statement, we approach the concept of Schlegel and Nowacki [7] who have neglected values even as high as 1,000 µg/100 ml as "negative" in monitoring investigations with the rapid method.

The Conference on Inorganic Lead recommended 10,000 µg/liter urine as the upper acceptable limit of ALA excretion [6]. On the basis of this value, the upper acceptable limit for the rapid method would, then, be about 1,700 µg/100 ml urine (1,250 ± 450).

Obviously the level of ALA excretion in the urine cannot be the sole guiding principle for medical prophylactic treatment in prevention of lead poisoning. It can be used only in combination with other applicable study methods, particularly the determination of the hemoglobin level.

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